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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/922,960	08/03/2001	Michael W. Leviten	R-441	9830

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EXAMINER	
BERTOGLIO, VALARIE E	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 01/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/922,960	LEVITEN, MICHAEL W.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,13-16 and 27-40* is/are pending in the application.

4a) Of the above claim(s) *1-4,13-16 and 27-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's amendment filed on 10/03/2003 has been entered. Claims 5-12 and 17-26 have been canceled. Claims 1-4, 13-16 and 27-29 are withdrawn as being drawn to nonelected subject matter. Claims 30-40 have been added. Claims 1-4, 13-16 and 27-40 are pending and claims 30-40 are under consideration in the instant action.

Election/Restrictions

This application contains claims 1-4, 13-16 and 27-29 drawn to an invention nonelected with traverse in Paper No. 13. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Priority

The amendment to the specification to render it consistent with the priority claimed on the oath has been noted.

Specification

The objection to the disclosure for being unclear in Example 1, *Embryonic Lethality*, (page 52) is maintained. The text discloses that at a stage where wild type and heterozygous mutant embryos are at embryonic development stage E8.5 having 6-9 formed somites, the homozygous mutants are arrested in development and have no somites formed (page 52, lines 13-14). However, Table 1 discloses that 3 homozygous mutant embryos from Litter 2 had 6-9 somites. The text of the specification is not consistent with the data in Table 1. Applicant argues that the appearance of 3 homozygous mutants with 6-9 somites (Litter 2, Table 1, page 52) does not indicate that these embryos are healthy or normal. This argument is off point. The text asserts

that homozygous mutant embryos do not form somites. Litter 2, Table 1, page 52 asserts that the embryos do form somites.

In light of applicant's arguments, the objections to the disclosure for being unclear in use of the symbol "/" (Table1, column 6) and the section titled "*Expression*" (page 52) are withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Newly added claims 30-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 30-40, being of similar subject matter to previously rejected claims 5-12 and 17-26, are rejected for reasons of record set forth on pages 6-8 of the previous office action.

Claims 30-40 are drawn to a transgenic mouse embryo or mouse, and cells or tissues derived from said mouse, whose genome comprises a disruption in the endogenous mouse ubiquitin ligase E3 gene. The claims encompass more than one ubiquitin ligase E3 gene, as there are multiple ubiquitin ligase E3 genes. While the specification and the art teaches that are several members of the ubiquitin ligase E3 gene superfamily (page 2, lines 7-15 and Rolfe, 1997, J. Mol. Med., Vol. 75, pages 5-17), the specification teaches only one, mouse ubiquitin ligase E3 gene

(SEQ ID NO:1) and its disruption in mouse. Therefore, adequate written description to support the claims of a transgenic mouse encompassing more than the one, disclosed ubiquitin ligase E3 gene disruption is lacking. It is maintained that the instant specification has only described the mouse ubiquitin ligase E3 gene as set forth in SEQ ID NO:1. Applicant argues that the specification clearly defines the ubiquitin ligase E3 gene on page 7, lines 5-15. While it is clear in the specification that disruption of only the sequence set forth in SEQ ID NO:1 is described, the claims, as written, broadly encompass more than the sequence set forth in SEQ ID NO:1.

As set forth by Perry (1998, Nature Genetics, Vol. 18, pages 143-146), disruption of a ubiquitin ligase E3 gene other than that set forth by SEQ ID NO:1 results in a vastly different phenotype with no obvious correlation to the phenotype effected by disruption of SEQ ID NO:1. The evidence of record offers no teachings of a relationship that would indicate a correlation between the phenotype effected by disruption of SEQ ID NO:1 and any other ubiquitin ligase E3 encompassed by the genus (refer to page 7-8 of the previous office action).

It was unknown as of Applicants' effective filing date that any mouse ubiquitin ligase E3 gene would have the same structural and functional properties as that encoded by SEQ ID NO:1. There is no evidence on the record of a relationship between the structures or function of the nucleotide sequences coding for any mouse ubiquitin ligase E3 gene and the nucleotide sequence set forth by SEQ ID NO:1 that would provide any reliable information about the structure or function of DNA molecules within the genus. The claimed invention as a whole is not adequately described if the claims require essential or critical elements that are not adequately described in the specification and that is not conventional in the art as of applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the

invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641,1646 (1998).

Therefore, the limited disclosure in the specification is not deemed sufficient to reasonably convey to one skilled in the art that Applicants were in possession of the huge genera recited in the claims at the time the application was filed. Therefore, only the ubiquitin ligase E3 gene encompassed by **SEQ ID NO:1**, but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph. University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that "to fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Thus it is concluded that the written description requirement is not satisfied for the claimed genera.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Amending the claims to read on the nucleotide sequence set forth by SEQ ID NO:1 may be sufficient to overcome this rejection.

Newly added claims 30-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The specification, while being enabling for a transgenic mouse embryo whose genome comprises a homozygous disruption in the endogenous mouse ubiquitin ligase E3 gene set forth by SEQ ID NO:1 wherein said embryo exhibits

embryonic lethality, does not reasonably provide enablement for a transgenic mouse or mouse embryo whose genome comprises a disruption in any endogenous mouse ubiquitin ligase E3 gene wherein the disruption is heterozygous. The previous rejections as they relate to newly added claims 30-40 are maintained for the reasons of record on page 8-13 of the previous office action mailed 03/27/2003, which are reiterated below.

Claims 30-40 are drawn to a transgenic mouse embryo (claim 30) or mouse (claims 31-40) comprising a heterozygous (claims 31-36 and 38-40) or homozygous disruption (claims 30-36 and 39) in the endogenous mouse ubiquitin ligase E3 genes, and cells or tissues derived from said mouse (claim 37).

Claims 31-37 encompass postnatal mice that are homozygous for a disruption in the ubiquitin ligase E3 gene (refer to previous office action, page 8, line 11-13). As disclosed in the specification, disruption of the ubiquitin ligase E3 gene leads to embryonic lethality, precluding the birth of the mice encompassed by the claims. The specification fails to teach how one of skill in the art can overcome the embryonic lethality associated with the claimed homozygous gene disruption to obtain the claimed mice and cells or tissues derived from the mice (claim 37). Applicant argues that the original claims have been cancelled, rendering the rejection moot, however, the newly added claims 31-40 read on the same invention encompassed previously rejected, and now canceled, claims.

Claims 30-40 broadly encompass heterozygous mice for a disruption in the ubiquitin ligase E3 gene (refer to previous office action, page 8, lines 18-21). Applicant argues that the original claims have been cancelled, rendering the rejection moot, however, the newly added claims 31-40 read on the same invention encompassed by the previously rejected, and now

canceled, claims. Furthermore, the functional limitation in the newly added claims, for example in claim 1, "wherein where the disruption is homozygous the transgenic mouse embryo ....exhibits increased incidence of lethality during embryonic development" does not limit the claimed subject matter to a homozygous mouse embryo. The specification fails to teach a phenotype, other than wild-type, for the claimed heterozygous mice. One of skill in the art would not know how to use the claimed heterozygous mice in any way other than a wild-type mouse.

Claims 30-40 broadly encompass multiple endogenous ubiquitin ligase E3 genes, however, the specification teaches disrupting only that set forth by SEQ ID NO:1 (refer to previous office action, page 8, lines 13-18). Applicant argues that is clear from the specification that the sequence is clearly defined in the specification such that it is clear which ubiquitin ligase E3 gene is being claimed. While it is the specification clearly sets forth that SEQ ID NO:1 was disrupted, the claims still encompass mouse ubiquitin ligase E3 genes other than that set forth by SEQ ID NO:1. As substantiated by the art (refer to Perry, 1998, Nature Genetics, Vol. 18, pages 143-146), disruption of ubiquitin ligase E3 genes other than that set forth by SEQ ID NO:1 results in a vastly different phenotype with no obvious correlation to the phenotype effected by disruption of SEQ ID NO:1.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 31-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 31-37 refer to "The transgenic mouse" of claim 30. Claim 30 is drawn to a mouse embryo. There is insufficient antecedent basis for "The transgenic mouse" in claim 30.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 5,6,8 and 9 under 35 U.S.C. 102(b) as being anticipated by Perry (1998, Nature Genetics, Vol. 18, pages 143-146) is maintained as it relates to newly added claims 30-40.

Claims 30-38 are drawn to a transgenic mouse embryo or mouse, and cells or tissues derived from said mouse, whose genome comprises a disruption in the endogenous mouse ubiquitin ligase E3 gene.

Perry taught a mouse comprising a disruption in the *Itch* locus, which is an ubiquitin ligase E3 gene.

The mouse of Perry exhibits phenotypes that differ from the claimed mouse. However, the since the mouse of Perry meets the instant claim limitations of a genome comprising a homozygous disruption of the endogenous mouse ubiquitin ligase E3 gene, any phenotypes associated with disruption of the ubiquitin ligase E3 gene are inherent properties of the mouse, since it does not appear that the mice are structurally different. Where the claimed and prior art

products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spade, 911F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433. See the M.P.E.P. 2112.01.

Applicant's arguments filed 10/03/2003 have been fully considered but they are not persuasive. Applicants have argued that Perry does not anticipate the claimed mouse because Perry does not teach a mouse having the same phenotypes as recited in the claims. See page 9 of the amendment.

In response, the Examiner asserts the claimed mouse and the mouse of Perry appear to be the same structurally; both comprise genomes that comprise homozygous disruptions of the endogenous ubiquitin ligase E3 gene. The Examiner further asserts that any phenotype associated with disruption of ubiquitin ligase E3 must be inherent to the mouse of Perry. **A product and its properties cannot be separated and the recognition of new properties does make and old product allowable.** As such, Perry anticipates all of the limitations of new claims 30-38.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 11 and 12 under 35 U.S.C 103(a) is withdrawn.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is 703-305-5469. The examiner can normally be reached on Mon-Fri 6:00-2:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on 703-305-4051. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Note: After January 13, 2004, the Examiner may be reached at (571) 272-0725, and should the Examiner be unavailable, inquiries may be directed to Deborah Reynolds, SPE of Art Unit 1632 at (571) 272-0734.

Valarie Bertoglio
Examiner
Art Unit 1632

PETER PARAS
PATENT EXAMINER